mental autoimmune encephalitis by showing location of the particle as seen by high resolution magnetic resonance could be confirmed with fluorescence microscopy.

Experimental autoimmune encephalitis was induced in SJL/J mice according to a proteolipid protein immunization protocol. When clinical signs of grade 2 disease were apparent, tail paralysis and limb weakness, the fluorscent anti-ICAM-1 antibody-conjugated paramanetic polymerized liposomes, as prepared in the prior example, were injected via a tail vein, 10 μL/g representing 1.2 mg/kg Gd^{+3} and 890 μg antibody/kg, and allowed to recirculate for 24 hours. Mice were then sacrificed and perfused with PBS. The brains were removed and cut in half sagitally, one half frozen for direct fluorscence microscope analysis of 10 μm thin sections and the other half fixed in 4% paraformaldehyde in PBS, pH7.4, and used for high resolution magnetic resonance imaging.

In three separate tests, a total of seven diseased mice were injected with fluorescent anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes and all were shown to be positive for the antibody conjugated-polymerized liposome binding to central nervous system vasculature by fluorescence microscopic analysis of cerebellum, brainstem and spinal cord. FIG. **33** is a typical fluorscence micrograph of mouse cerebellum counterstained with haematoxylin showing multiple vessels surrounded by an inflammatory infiltrate. Anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes, indicated by arrows, are seen by fluorescence to be bound to small capillaries (SV), but not bound to large central arteriole (LV) which is seen to be negative for fluorescence. This is consistent with expression of ICAM-1 which is upregulated on endothelium of venules and capillaries, but not expressed on arterioles or larger vessels. We also noted fluorescent anti-ICAM-l polymerized liposomes bound to microvessels that are not associated with inflammatory infiltrates, which is consistent with histological findings of ICAM-1 expression on both infiltrated and non-infiltrated vessels.

Six controls: three healthy animals injected with anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes; two diseased animals administered anti-trinitrophenol antibody-conjugated paramagnetic polymerized liposomes, and one diseased animal administered anti-Vβ11 T-cell receptor antibody-conjugated paramagnetic polymerized liposomes, targeted to an antigen not expressed in the SJL/J mouse, were all found by fluorescence microscopy to show no polymerized liposome binding.

EXAMPLE XII

High resolution magnetic resonance images were made of the complimentary half of two mouse brains from mice having grade 2 experimental autoimmune encephalitis used in the previous example containing anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes. High resolution T1 and T2-weighted images of the intact half brains were obtained by using a 9.4T MR scanner (General Electric) using 3DFT spin echo pulse sequences. Parameters for T1-weighted images were TR 200 ms, TE 4 ms, 1 NEX, matrix 256×256×256, and a field of view of 1 cm, resulting in a voxel size of approximately 40 μm in each dimension. T1-weighted acquisitions times were approximately 7 hours per scan. T2-weighted parameters were TR 1000 ms, TE 20 ms, 8 NEX, matrix 256×256×256. T2-weighted scan times were approximately 12 hours. FIG. **34** shows a T2-weighted scan of an experimental autoimmune encephalitis mouse, without injection of polymerized liposomes, cerebrum (coronal) and cerebellum (axial) to define normal anatomy. FIG. **35** shows a representative slice from a Ti-weighted scan of an autoimmune encephalitis mouse injected with anti-ICAM-1 antibody-conjugated paramagetic polymerized liposomes. Diffuse perivascular enhancement is seen throughout the brain, in the cerebellum and cerebrum, lending particularly significant contrast between the meagerly vascularized cerebellar white (W) and the highly vascular grey (g) matter. FIG. **36** shows a representative slice from a T1-weighted scan of a healthy mouse similarly injected with anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes showed no enhancement.

Signal intensity measurements were made using the image analysis program Voxel View/Ultra 2.2 (Vital Images, Inc., Fairfield, Iowa). For each mouse brain, three slices were chosen for analysis. For each slice, the signal intensity of cerebral gray, cerebellar gray, and cerebellar white matter was determined by manually drawing at least five large region-of-interest paths within each of these tissues. Signal intensity measurements from the three slices were averaged to give a mean signal intensity value for each tissue type, means weighted according to standard deviation of individual signal intensity values. The differences in tissue signal intensities between mouse brains were assessed using the two-tailed Stundent's t-test. The statistical significance level was set at $P<0.05$. The results are shown in FIG. **37**. Compared to the controls, the magnetic resonance scans of the experimental autoimmune encephalytis infected mice injected with anti-ICAM-1 antibody-conjugated paramagnetic polymerized liposomes showed substantial increases in magnetic resonance signal intensity of about 32% in the cerebellar, 28% in the cerebral cortex and, to a lesser extent, about 18% in the cerebellar white matter. As a result of the enhanced gray matter signal, contrast between gray and white matter was improved. This was particularly pronounced in the cerebellum which was actively affected by experimental autoimmune encephalytis.

The above examples have demonstrated that antibody-conjugated paramagnetic polymerized liposomes can be delivered to cell adhesion molecules upregulated in disease. This provides a new target-specific magnetic resonance contrast enhancement agent for providing in vivo imaging studies of specific targeted physiological activies, such as, for example, endothelial antigens involved in numerous pathologies.

While in the foregoing specification this invention has been described in relation to certain preferred embodiments thereof, and many details have been set forth for purpose of illustration it will be apparent to those skilled in the art that the invention is susceptible to additional embodiments and that certain of the details described herein can be varied considerably without departing from the basic principles of the invention.

We claim:

1. A lipid composition comprising a plurality of particles each comprising a lipid sheet containing lipids with at least one hydrophobic tail group that is covalently cross-linked with a hydrophobic tail group of an adjacent lipid, each particle further comprising a targeting agent attached to hydrophilic head groups of a portion of lipids in the lipid sheet, each particle further comprising a substance for delivery to a target tissue.

2. A lipid composition according to claim **1**, wherein the substance is a treatment agent.

3. A lipid composition according to claim **2**, wherein the treatment agent is attached to the particle.

4. A lipid composition according to claim **2**, wherein the treatment agent is encapsulated within the particle.